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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/560,968 | 03/19/2007 | Michael Josephus Van Eijk | VAN EIJK17 | 2423 |

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| EXAMINER | |
|---|---|
| TUNG, JOYCE | |
| ART UNIT | PAPER NUMBER |
| 1637 | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/560,968 | VAN EIJK, MICHAEL JOSEPHUS | |
| | Examiner | Art Unit | |
| | Joyce Tung | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *120409*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *32 and 35-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32 and 35-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

The response filed 12/04/09 to the Office action has been entered. Claims 32, and 35-72 are pending.

1. The rejection of claims 39-48 and 53 under 35 U.S.C. 112, second paragraph is withdrawn because of the amendment of the claims.

2. Claims 32, 35-41, 44-52, 54-56 and 58-60 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hogan et al. (5424413, issued, Jun. 13, 1995).

Hogan et al. disclose a nucleic acid hybridization probe and method of use. The probe comprises two separate target-specific regions that hybridize to a target nucleic acid sequence and at least two distinct arm regions that do not hybridize with the target nucleic acid but possess complementary regions that are capable of hybridizing with one another (see column 1, lines 51-58 and fig. 2A) to form a duplex in the presence of target nucleic acid (see column 1, lines 58-66 and column 2, lines 59-62). The duplex has a Tm at least $4^0$C (or $7^0$C or even $10^0$C) which is greater than the hybridization temperature to a target nucleic acid (see column 2, lines 60-63). The GC content of both arms ranges from 50%-100% (see fig. 2A). The GC content of some arms is more than 60% (see fig. 3A, 132 strand) and 70% (see fig. 3B, 135 strand). C1 or C2 comprises at least one C nucleotide more than C nucleotides in T1 or T2 (see fig 2A, strand 2) or at least two, three or four G nucleotides more than G nucleotides in T1 or T2 (see fig. 2A, strand 1) or at least five G nucleotides more than G nucleotides in T1 or T2 (see fig. 18, strand 1). The strand of the probe has chemically modified bases (see column 2, lines and column 6, lines 10-19). The length of the arm is 8 to 20 contiguous complementary bases (see column 8, lines 9-11). The arm region is designed to have a site for extension by a polymerase (see column 21, lines

46-48 and column 38, lines 40-44). The regions which are complementary to a target nucleic acid include a variety of mismatches in which some of the mismatches are located at the end of the strands (see fig. 13 and column 19, lines 47-50). Hogan et al. also disclose a set of nucleic acid probes which comprises three probes in which the 135 strand is interpreted as a third probe having a target hybridization region and an additional mismatch and a third probe is distinct from another two probes (see fig. 7). In one system, arm region duplex formation comprises an active restriction enzyme cleavage site (see column 21, lines 10-12). A group of nucleic acid probes is disclosed in which at least two pairs of probes are involved (see fig. 6C, 6D, fig. 7). Each arm region of the probe has a unique sequence since the sequence of each arm region is not identical so that they form a unique combination (see fig. 7). A target is a nucleic acid sequence including essential sequences within the genome of a pathogenic organism, essential mRNA sequences produced by a pathogenic organism, and essential sequences within cancer cells (see column 4, lines 60-64).

Based on the analysis above, the teachings of Hogan et al. anticipate the limitations of the claims.

The response argues that based upon the amendment of claim 32, claim 32 and its dependent claims are now novel over Hogan et al. However, the newly added wherein clause is directed to intended use. The instant claims are drawn to a pair of oligonucleotide probes with the elements as recited in the claims. The target nucleic acid D is not a part of the probe, but is intended to be used along with said probe. Intended use does not have patentable weight in product claims. Hogan et al. disclose each element of the probes as claimed. Therefore, the teachings of Hogan et al. anticipate the limitations of the claims. The rejection is maintained.

3. Claims 42-43, 57, 61-72 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hogan et al. (5424413, issued, Jun. 13, 1995) as applied to claims 32, 35-41, 44-52, 54-56 and 58-60 above in view of Zhang et al. (5,876,924, issued March 2, 1999).

The teachings of Hogan et al. are set forth in section 2 above. Hogan et al. do not disclose a junction site between S1 and S2 as recited in claim 57 and the method step (c) and (d) for detection of a target nucleic acid in a sample as recited in claims 61-63, and 67.

Zhang et al. disclose an improved method which allows for rapid, sensitive and standardized detection and quantitation of nucleic acids from pathogenic samples from a patient (see column 3, lines 11-15). The method applies a pair of non-overlapping oligonucleotide amplification probes (see column 3, lines 62-66). These probes are referred as a capture/amplification probe and an amplification probe (see column 3, lines 66-67) and are complementary to adjacent regions of a target (see column 4, lines 3-8) and do not overlap one another (see column 4, lines 8-9). The two probes join together by a ligating agent (see column 4, lines 9-11). The ligated amplification sequence is directly detected (see column 4, lines 16-19). The two amplification probes may be ligated to form contiguous sequence to be amplified (see column 4, lines 24-26). The polymerase chain reaction products are subject to electrophoresis for detection (see column 16, lines 25-35).

One of ordinary skill in the art would have been motivated to construct a probe comprising the terminal segments of the probe as taught by Zhang et al. which are able to be ligated when the terminal segments are hybridized to a target nucleic acid sequence at an adjacent position because the assembly of an amplifiable DNA by ligation increases specificity and makes possible a detection of a single mutation in a target (see column 3, lines 33-33). It

would have been prima facie obvious to construct a terminal on each oligonucleotide probe which is able to be ligated when the terminal is hybridized to a target nucleic acid sequence at an adjacent position.

In addition, one of ordinary skill in the art would have also been motivated to apply an amplification method for detecting a target nucleic acid as taught by Zhang et al. because the method of Zhang et al. is an improved method which allows for rapid sensitive detection and can be performed in microtubes or a micro-well plate (see column 3, lines 19-27). It would have been prima facie obvious to perform the steps as recited in claims 61-69.

Hogan et al. do not disclose the limitations of claims 42-43 that the GC content in the arm region is higher than 80% or between 90% and 100%.

The capture/amplification probe designed for the method has a GC content at least 60%, and as such that they exhibit minimal secondary structure e.g. hairpin or fold back structure (see column 36, lines 1-3).

One of ordinary skill in the art would have been motivated to design an oligonucleotide probe comprising a GC content which is higher than 80% or between 90% and 100% as taught by Zhang et al. because by doing do so they exhibit minimal secondary structure e.g. hairpin or fold back structure (see column 36, lines 1-3). It would have been prima facie obvious to design an oligonucleotide probe which has a GC content which is higher than 80% or between 90% and 100%.

Hogan et al. do not disclose a kit comprising probes and reagents for detection of a target DNA sequence in a sample as recited in claims 70-72.

Zhang et al. disclose a kit which comprises probes and reagents for detection of an amplified ligated DNA sequences (see column 25, lines 7-36).

One of ordinary skill in the art would have been motivated to construct a kit including probes and reagents as taught by Zhang et al. because it was routine practice in the art for conveniently performing a method. It would have been prima facie obvious to construct a kit as claimed.

As discussed above, the 35 U.S.C. 102 rejection of claim 32 and its dependent claims as anticipated by Hogan et al. is maintained with the reasons set forth above.

The response argues that Zhang et al. do not disclose that the capture/amplification probes contain any a GC rich region that could serve as a "clamp", Zhang only disclose one end of the probe to be GC rich. However, the teachings of Zhang et al. provided herein disclose the benefit of using GC rich regions (see column 36, lines 1-3). Therefore one of ordinary skill in the art would have been motivated to design an oligonucleotide probe comprising a GC content which is higher than 80%, or between 90% and 100%, in clamp regions.

Based upon the analysis above, the rejection is maintained.

**Summary**

4. No claims are allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

/Joyce Tung/
Examiner, Art Unit 1637
Feb. 4, 2010